

REMARKS

The Office Action of May 1, 2003 has been received and reviewed. Claims 1, 3-6, 9, 10 and 12 are pending in the application and all claims stand rejected. Claims 1 and 3 have been amended as set forth herein. All amendments are made without prejudice or disclaimer. Reconsideration is respectfully requested.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 1, 3-6 and 9-12 stand rejected under 35 U.S.C. § 112, second paragraph, as assertedly being indefinite. Applicants respectfully traverse the rejections as hereinafter set forth.

Specifically, it was thought that the recitation of "after administration to a subject" was unclear as to what is being administered to the subject. Although applicants do not agree that the phrase is indefinite, claim 1 has been amended to recite in part "after administration of the vaccine to the subject" to clarify that the vaccine containing the antigen is being administered to the subject. The amendment to claim 1 is merely cosmetic since the amendment merely indicates that the vaccine, which includes the antigen and the peptide carrier compound, is administered to the subject.

The recitation of "physiological conditions" of claim 1 was also thought to be vague. Although applicants do not agree that the phrase "physiological conditions" is vague, to expedite prosecution, claim 1 has been cosmetically amended to recite in part "physiological conditions of a subject." Thus, it should be clear that the thioester bond dissociates under physiological conditions of a subject to which the vaccine is administered.

Claim 3 was thought to be vague and indefinite for reciting "protein" and "polypeptide." Although applicants do not agree that claim 3 is indefinite, the recitation of "a polypeptide" has been removed.

Accordingly, reconsideration and withdrawal of the indefiniteness rejections of claims 1, 3-6 and 9-12 are requested.

Rejections under 35 U.S.C. § 102

Claims 1, 3, 4 and 12 stand rejected under 35 U.S.C. § 102(e) as assertedly being anticipated by Yatvin et al. Applicants respectfully traverse the rejections as set forth herein.

Claim 1 is not anticipated since Yatvin et al. does not disclose each and every element of claim 1. Claim 1 is directed to a “vaccine comprising an antigen and a fatty acid or fatty acid-peptide carrier compound which are directly linked by a thioester bond that is labile and dissociates under physiological conditions of a subject, wherein said antigen dissociates from said fatty acid or fatty acid-peptide carrier compound after administration of the vaccine to the subject.”

Yatvin et al. does not disclose a vaccine as required by claim 1. As known in the art, a vaccine is a preparation of an antigen(s) to elicit an immune response. As stated in Yatvin et al. “the present invention is directed to an improved method for delivering biologically-active compounds to phagocytic cells and cellular organelles.” (Yatvin et al., Col. 7, lines 30-33).

Yatvin et al. also does not disclose an antigen directly linked to a fatty acid or fatty acid-peptide carrier compound by a thioester bond. As stated in Yatvin et al., “the present invention provides compositions of matter and methods for facilitating the entry biologically-active compounds into phagocytic cells.” (*Id.* at Col. 17, lines 63-65). Yatvin et al. goes on to define “biologically-active compound” as encompassing “all naturally-occurring or synthetic compounds capable of eliciting a biological response or having an effect, either beneficial or cytotoxic, on biological systems, particularly cells and cellular organelles. These compounds are intended to include but are not limited to all varieties of drugs ... as well as peptides including antimicrobial peptides.” (*Id.* at Col. 2, line 66-Col. 3, line 8). There is no mention of a vaccine or a vaccine including an antigen directly linked by a thioester bond to a fatty acid or a fatty acid-peptide carrier included as a biologically-active compound.

The Office Action states the “weak linker functionality which is cleaved inside phagocytic cells under specific conditions is thioester (see paragraph bridging columns 22 and 23).” (Office Action of May 1, 2003, page 6). The relevant portion of Yatvin et al. recites “[t]he weak functionalities [used to link the polar lipid moiety or biologically-active agent to the specific linker moiety] include, but are not limited to phosphoramidate, phosphodiester, carbonate,

amide, carboxyl-phosphoryl anhydride, ester and thioester.” (Yatvin et al. at Col. 23, lines 1-4). However, the disclosure is non-enabling since none of the working examples of Yatvin et al. actually disclose an **antigen** linked to a fatty acid or fatty-acid peptide carrier with a **thioester** bond as is required by the claims.

The Office Action further refers to Example II of Yatvin et al. for the asserted disclosure of an antigenically active peptide. (*See, Office Action* at page 6). However, Example II does not disclose an **antigen** linked to a fatty acid or a fatty acid-peptide carrier by a **thioester** bond. Example II indicates that the reaction scheme used to produce an anti-viral compound (not an antigen) conjugated to sphingosine is illustrated in FIG. 2. (*See, Yatvin et al.* at Example 2). FIG. 2 does not illustrate a thioester bond in any of the chemical structures. Thus, Yatvin et al. does not anticipate claim 1. Claims 3, 4 and 12 are not anticipated, at the very least, as depending from novel independent claim 1.

Accordingly, reconsideration and withdrawal of the anticipation rejections of claims 1, 3, 4 and 12 are requested.

Rejections under 35 U.S.C. § 103

Claims 1, 3-5, 9, 10 and 12

Claims 1, 3-5, 9, 10 and 12 stand rejected under 35 U.S.C. § 103(a) as assertedly being unpatentable over Chang et al. in view of Yatvin et al. Applicants respectfully traverse the rejections as set forth herein.

A *prima facie* case of obviousness cannot be established since no suggestion or motivation exists to combine the cited references. In fact, Chang et al. teaches away from Yatvin et al. As stated by the Federal Circuit, “a reference will teach away if it suggests that the line of development flowing from the reference’s disclosure is unlikely to be productive of the result sought by the applicant.” (*In re Gurley*, 27 F.3d 551, 553, 31 USPQ2d 1130, 1131 (Fed. Cir. 1994)). Yatvin et al. discloses the delivery of a biologically-active compound to “phagocytic cells through conjugating the compound with a microparticle via a **cleavable** linker moiety.” (Yatvin et al. at Col. 7, lines 44-45) (emphasis added). Chang et al. discloses the linking of a membrane blending agent to a macromolecular drug and as stated in Chang et al. “[u]sually, the

membrane blending agent is **irreversibly** linked to the drug.” (Chang et al. at Col. 5, lines 31-32) (emphasis added). Since Chang et al. discloses the use of an **irreversible** linkage between the membrane blending agent and the drug, one of ordinary skill in the art would not be motivated to combine the teaching of Chang et al. with Yatvin et al. that uses a **cleavable** linker moiety between the biologically-active compound and the microparticle.

A *prima facie* case of obviousness also cannot be established since the cited references do not, alone or in combination, teach or suggest each and every element of independent claim 1. Neither Chang et al. nor Yatvin et al. teach or suggest the preparation of a vaccine. As stated in Chang et al. “[t]his invention pertains to improved compositions and methods for enhancing the association of macromolecular drugs with cell membranes and for enhancing the association and entry of macromolecular drugs into cells in order to improve drug efficacy.” (Chang et al. at Col. 1, line 66 through Col. 2, line 2). Yatvin et al. does not teach or suggest the preparation of a vaccine, but rather states “the present invention provides compositions of matter and methods for facilitating the entry biologically-active compounds into phagocytic cells.” (Yatvin et al. at Col. 17, lines 63-65).

Further, neither Chang et al. nor Yatvin et al. teaches or suggests an **antigen** linked to a fatty acid or fatty-acid peptide carrier with a **thioester** bond as required by claim 1. As stated in the Office Action “Chang et al. [does not] us[e] a thioester bond as the labile bond.” (Office Action at page 7). Yatvin et al. does not contain an enabling disclosure of a thioester bond since none of the working examples of Yatvin et al. actually disclose an antigen linked to a fatty acid or antigen linked to a fatty-acid peptide carrier with a thioester bond. “In order to render a claimed apparatus or method obvious, the prior art must enable one skilled in the art to make and use the apparatus or method.” (*Beckman Instruments Inc. v. LKB Produkter AB*, 892 F.2d 1547, 1551, 13 USPQ2d 1301, 1305 (Fed. Cir. 1989).

One of ordinary skill in the art also would not have a reasonable expectation of success in combining the teachings of Chang et al. with the teachings of Yatvin et al. The bond between the membrane blending agent and the macromolecular drug of Chang et al. is irreversible. The Office Action indicates “it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to replace Chang’s disulfide linkage with Yatvin’s

alternative, labile or cleavable thioester linkage, to produce the composition of the instant invention, with a reasonable expectation of success.” (Office Action at page 7). However, the disulfide bond of Chang et al. is not located between the membrane blending agent and the macromolecular drug, but is between the membrane blending agent and a blocking agent. (*See, Chang et al.* at Col. 6, lines 26-31). Unlike the claimed antigen of the vaccine of claim 1, the blocking agent of Chang et al. preferably “does not induce immune responses in humans.” (*Id.* at Col. 6, lines 6-7). Thus, one of ordinary skill in the art would not be motivated to combine the referenced and would not expect the irreversible bond between the membrane blending agent and the macromolecular drug of Chang et al. to function in the same manner as the cleavable linker moiety between the biologically-active compound and the microparticle of Yatvin et al.

Thus, claim 1 is not obvious in view of the cited references. Claims 3-5, 9, 10 and 12 are not obvious, at the very least, as depending from non-obvious independent claim 1. (*See, In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)).

Reconsideration and withdrawal of the obviousness rejections of claims 1, 3-5, 9, 10 and 12 are requested.

Claims 1, 3-5 and 12

Claims 1, 3-5 and 12 stand rejected under 35 U.S.C. § 103(a) as assertedly being unpatentable over Shen et al. in view of Yatvin et al. Applicants respectfully traverse the rejections as set forth herein.

A *prima facie* case of obvious cannot be established since neither Shen et al. nor Yatvin et al., alone or in combination, teaches or suggests all of the elements of independent claim 1. For instance, neither Shen et al. nor Yatvin et al. teaches or suggests a vaccine. Shen et al. is limited to “fatty acid-conjugated products with a disulfide linkage [that] are employed for delivery of the sulfhydryl-containing compounds to mammalian cells” and does not suggest or motivate a vaccine. (*Shen et al.*, Col. 4, lines 63-65). Further, Yatvin et al. does not teach or suggest a vaccine, but is limited to “compositions of matter and methods for facilitating the entry biologically-active compounds into phagocytic cells.” (*Yatvin et al.* at Col. 17, lines 63-65).

Further, neither Shen et al. nor Yatvin et al. teaches or suggests an antigen directly linked to a fatty acid or fatty acid-peptide carrier compound by a thioester bond. Shen et al. is limited to the use of disulfide linkages (*See, Shen et al.* at Col. 5, line 34) and Yatvin et al. does not teach or suggest an enabling disclosure of a thioester bond in any of the working examples, but rather only mentions a thioester bond in a laundry list of possible bonds (*e.g.*, "phosphoramidate, phosphodiester, carbonate, amide, carbonyl-phosphoryl anhydride, ester and thioester.") (*Yatvin et al.* at Col. 23, lines 1-4). As stated by the Federal Circuit "[i]n order to render a claimed apparatus of method obvious, the prior art must enable one skilled in the art to make and use the apparatus or method." (*Beckman Instruments, Inc., v. LKB Produkter AB, supra*). Since Yatvin et al. has not enabled a thioester bond and Shen et al. does not teach or suggest a thioester bond, a *prima facie* case of obviousness cannot be established with regard to independent claim 1.

Claims 3-5 and 12 are non-obvious at the very least as depending from non-obvious independent claim 1. (*See, In re Fine, supra*).

Thus, reconsideration and withdrawal of the obviousness rejections of claims 1, 3-5 and 12 are requested.

Claim 6

Claim 6 stands rejected under 35 U.S.C. § 103(a) as assertedly being unpatentable over Chang et al. or Shen et al. as modified by Yatvin et al. as applied to claims 1, 3, and 4, and further in view of Russell-Jones et al. or Meloen et al. Applicants respectfully traverse the rejections as set forth herein.

Claim 6 is non-obvious, at the very least, as depending from non-obvious independent claim 1. (*See, In re Fine, supra*). With further regard to claim 6, a *prima facie* case of obviousness cannot be established since the cited references do not, singly or in combination, teach or suggest each and every element of claim 6. For instance, none of the cited references teaches or suggests a peptide having the exact amino acid sequence of SEQ ID NO: 1 as required to establish a *prima facie* case of obviousness.

Thus, reconsideration and withdrawal of the obviousness rejection of claim 6 is requested.

CONCLUSION

In view of the amendments and remarks presented herein, applicants respectfully submit that the amended claims define patentable subject matter. If questions should remain after consideration of the foregoing, the Examiner is kindly requested to contact applicants' attorney at the address or telephone number given herein.

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